

**AMENDMENTS TO THE CLAIMS**

**IN THE CLAIMS:**

The following claim listing is meant to replace all previous claim listings.

1. (Withdrawn) A method for the design and/or the selection of chemokines variants having agonist or antagonist property towards a ligand of GPCR of animal cells comprising the following steps:
  - A) obtaining a phage displayed library expressing on their surface said chemokine variants mutated within the domain responsible for their effector function,
  - B) having a culture of animal cells expressing on their membranes the GPCR,
  - C) Incubating the cell culture with the phage library obtained in A),
  - D) harvesting the cells after removal of non specifically bound and surface receptor bound phages,
  - E) Releasing the phages internalized in step C) by lysis of cells obtained in D)
  - F) Infecting an *E. coli* culture with the released phages obtained in E) and amplifying the clones previously internalized ,
  - G) Obtaining a phage library enriched in internalizing chemokines ligands,
  - H) Assaying the agonist or antagonist property of the chemokine variants versus the native one. <sup>C</sup>
2. (Withdrawn) The method according to claim 1 wherein the chemokine is RANTES.
3. (Withdrawn) The method according to claim 1 wherein the GPCR expressed within the membrane of animal cells is CCR5.

4. (Withdrawn) The method according to claim 1 wherein the animal cells are human cells.

5. (Withdrawn) The method according to claim 2 wherein the phage library of RANTES variants is obtained using a method comprising the following steps:

- Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
- Performing a PCR mutagenesis of the 5' portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,
- Inserting the purified PCR products into a phage display vector,
- Production of the phage library by introducing the vector containing the purified PCR products into an *E. coli* culture.

6. (Withdrawn) The method according to claim 2 wherein anti-HIV activity is assayed.

7. (Withdrawn) A method for the design and/or the selection of chemokines having agonist or antagonist property towards a GPCR of animal cells comprising the following steps:

- A. obtaining a phage displayed library expressing on their surface said chemokine mutated within the domain responsible for their effector function
- B. having a culture of animal cells expressing on their membranes the GPCR,
- C. Incubating the cell culture with the phage library obtained in A),
- D. Eliminating the non specifically bound phages from the cells, by a process keeping the specifically bound phages on the said receptor

- E. Incubating the cells obtained in D) with an *E. coli* culture and amplifying the clones being infected by the phages bound to the said receptor on animal cells,
- F. Obtaining a phage library enriched in externally bound phages,
- G. Assaying the agonist or antagonist property of the chemokine variants versus the native chemokine.

- 8. (Withdrawn) The method according to claim 7, wherein the chemokine is RANTES.
- 9. (Withdrawn) The method according to claim 7, wherein the GPCR expressed within the membrane of animal cells is CCR5.
- 10. (Withdrawn) The method according to claim 7, wherein the animal cells are human cells.
- 11. (Withdrawn) The method according to claim 8, wherein the phage library of RANTES variants is obtained using a method comprising the following steps:
  - Obtaining a DNA sequence coding for human RANTES resulting from the amplification of cDNA prepared from activated PBMCs,
  - Performing a PCR mutagenesis of the 5' portion of the DNA sequence of RANTES using a specific downstream primer and a degenerate upstream primer containing recognition sites for restriction enzymes in order to insert the PCR amplification products into the phage display vector,

- Inserting the purified PCR products into a phage display vector,
- Production of the phage library by introducing the vector containing the purified PCR products into an E. coli culture.

12. (Withdrawn) The method according to claim 8 wherein anti-HIV activity is assayed.

13. (Currently Amended) A compound comprising the following formula: ~~XaaSPXaa~~  
~~Xaa, Xaa, Xaa (SEQ ID NO: 40)~~ Xaa Ser Pro Xaa Ser Ser Gln Xaa Xaa Xaa – RANTES 10-68  
 (SEQ ID NO: 41) in which

- Xaa at position 1 is L or an aromatic residue,
- Xaa at position 4 is L, M or V
- Xaa at position 8-10 is S, P, T or A.

14. (Previously Presented) The compound according to claim 13 having one of the following formulae :

LSPVSSQSSA	(SEQ ID NO: 1) (P <sub>1</sub> )
FSPLSSQSSA	(SEQ ID NO: 2) (P <sub>2</sub> )
LSPMSSQSPA	(SEQ ID NO: 3)
WSPLSSQSPA	(SEQ ID NO: 4)
WSPLSSQSSP	(SEQ ID NO: 5)
LSPLSSQSAA	(SEQ ID NO: 15)
YSPLSSQSSP	(SEQ ID NO: 17)

15. (Withdrawn) The compound according to claim 13 having the formula:

FSPLSSQSSA(SEQ ID N): 2-RANTES(10-68).

16.(Withdrawn) The compound according to claim 13 having the formula:  
LSPVSSQSSA-RANTES (10-68).

17.(Currently Amended) A pharmaceutical composition which comprises of a compound having the formula: ~~XaaSPXaa-Xaa, Xaa, Xaa (SEQ ID NO:40)~~ Xaa Ser Pro Xaa Ser Ser Gln Xaa Xaa Xaa – RANTES 10-68 (SEQ ID NO: 41) in which

- Xaa at position 1 is L or an aromatic residue,
- Xaa at position 4 is L, M or V
- Xaa at position 8-10 is S, P, T or A.

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

18.(Withdrawn) The composition of claim 17, in which the compound have the formula:  
LSPVSSQSSA(SEQ ID NO: 1)- RANTES(10-68).

19.(Withdrawn) The composition of claim 17, in which the compound have the formula:  
FSPLSSQSSA (SEQ ID NO:2) -RANTES-(10-68).

20.(Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 18.

21.(Withdrawn) A method for preventing and/or inhibiting HIV infection in humans comprising a step of treatment with a composition of claim 19.

22.(Withdrawn)A method for preventing and/or curing inflammatory or malignant diseases in humans comprising a step of treatment with a composition of claim 13 or 14.

23. (Previously Presented) A compound comprising one of the following formulae :

LSPQSSLSSS	(SEQ ID NO: 6),
ASSGSSQSTS	(SEQ ID NO: 7),
ISAGSSQSTS	(SEQ ID NO: 8),
RSPMSSQSSP	(SEQ ID NO: 9),
YSPSSSLAPA	(SEQ ID NO: 10),
MSPLSSQASA	(SEQ ID NO: 11),
ASPMSSQSSS	(SEQ ID NO: 12),
QSPLSSQAST	(SEQ ID NO: 13),
QSPLSSTASS	(SEQ ID NO: 14),
GSSSSSQTPA	(SEQ ID NO: 16),
FSSVSSQSSS,	(SEQ ID NO: 18),
VSTLSSPAST,	(SEQ ID NO: 30) ,
ASSFSSRAPP,	(SEQ ID NO: 31),
QSSASSSSSA	(SEQ ID NO: 32),
QSPGSSWSAA,	(SEQ ID NO: 33),
QSPSSWSSS,	(SEQ ID NO: 34),
QSPLSSFTSS,	(SEQ ID NO: 35) and
ASPQSSLPAA,	(SEQ ID NO: 36).

24. (Previously Presented) A compound consisting essentially of one of the following formulae :

LSPQSSLSSS	(SEQ ID NO: 6),
ASSGSSQSTS	(SEQ ID NO: 7),
ISAGSSQSTS	(SEQ ID NO: 8),
RSPMSSQSSP	(SEQ ID NO: 9),
YSPSSSLAPA	(SEQ ID NO: 10),
MSPLSSQASA	(SEQ ID NO: 11),
ASPMSSQSSS	(SEQ ID NO: 12),
QSPLSSQAST	(SEQ ID NO: 13),
QSPLSSTASS	(SEQ ID NO: 14),
GSSSSSQTPA	(SEQ ID NO: 16),
FSSVSSQSSS,	(SEQ ID NO: 18),
VSTLSSPAST,	(SEQ ID NO: 30),
ASSFSSRAPP,	(SEQ ID NO: 31),
QSSASSSSSA	(SEQ ID NO: 32),
QSPGSSWSAA,	(SEQ ID NO: 33),
QSPSSWSSS,	(SEQ ID NO: 34),
QSPLSSFTSS,	(SEQ ID NO: 35) and
ASPQSSLPAA,	(SEQ ID NO: 36).

25. (Previously Presented) A pharmaceutical composition which comprises one of the following formulae:

LSPQSSLSSS	(SEQ ID NO: 6),
ASSGSSQSTS	(SEQ ID NO: 7),
ISAGSSQSTS	(SEQ ID NO: 8),
RSPMSSQSSP	(SEQ ID NO: 9),
YSPSSSLAPA	(SEQ ID NO: 10),

MSPLSSQASA (SEQ ID NO: 11),  
ASPMSSQSSS (SEQ ID NO: 12),  
QSPLSSQAST (SEQ ID NO: 13),  
QSPLSSTASS (SEQ ID NO: 14),  
GSSSSSQTPA (SEQ ID NO: 16),  
FSSVSSQSSS, (SEQ ID NO: 18),  
VSTLSSPAST, (SEQ ID NO: 30),  
ASSFSSRAPP, (SEQ ID NO: 31),  
QSSASSSSSA (SEQ ID NO: 32),  
QSPGSSWSAA, (SEQ ID NO: 33),  
QSPSSWSSS, (SEQ ID NO: 34),  
QSPLSSFTSS, (SEQ ID NO: 35) and  
ASPQSSLPAA, (SEQ ID NO: 36).

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.

26. (Previously Presented) A pharmaceutical composition consisting essentially of one of the following formulae:

LSPQSSLSSS (SEQ ID NO: 6),  
ASSGSSQSTS (SEQ ID NO: 7),  
ISAGSSQSTS (SEQ ID NO: 8),  
RSPMSSQSSP (SEQ ID NO: 9),  
YSPSSSLAPA (SEQ ID NO: 10),  
MSPLSSQASA (SEQ ID NO: 11),  
ASPMSSQSSS (SEQ ID NO: 12),  
QSPLSSQAST (SEQ ID NO: 13),  
QSPLSSTASS (SEQ ID NO: 14),  
GSSSSSQTPA (SEQ ID NO: 16),  
FSSVSSQSSS, (SEQ ID NO: 18),



VSTLSSPAST, (SEQ ID NO: 30),  
ASSFSSRAPP, (SEQ ID NO: 31),  
QSSASSSSSA (SEQ ID NO: 32),  
QSPGSSWSAA (SEQ ID NO: 33),  
QSPSSWSSS, (SEQ ID NO: 34),  
QSPLSSFTSS, (SEQ ID NO: 35) and  
ASPQSSLPAA, (SEQ ID NO: 36).

or a pharmaceutical salt thereof, in a mixture with one or more pharmaceutically acceptable excipient.